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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/390,851	09/07/1999	HENRIK PEDERSEN	5655.204-US	7651

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[REDACTED] EXAMINER

FRIEND, TOMAS H F

ART UNIT	PAPER NUMBER
1627	19

DATE MAILED: 04/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

file copy

Application N .

09/390,851

Applicant(s)

PEDERSEN ET AL.

Examiner

Tomas Friend

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 23 January 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 28-55 is/are pending in the application.
 - 4a) Of the above claim(s) 40-47 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 28-55 is/are rejected.
- 7) Claim(s) 35,36 and 54 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5,6</u> . | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Change of Examiner's Name

The name of the examiner of this application has changed from Thomas Prasthofer to Tomas Friend.

Status of the Application

Receipt is acknowledged of a response to a restriction requirement on 23 January 2002 (Paper No. 18).

Status of the Claims

Claims 28-55 are pending in the present application. Claims 40-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 18. Claims 28-39 and 48-55 are pending and examined on their merits.

Response to Restriction and Election of Species

Applicants' election without traverse of Group I, claims 28-39, 48, and 50-55 in Paper No. 18 is acknowledged. Also acknowledged is applicants' election of species A-protease; B-phage; C-protease substrate; D-immobilization; E-covalent attachment; F-PEG; and G-phage-peptide.

Objections to the Specification

1. The specification is objected to for containing numerous typographical, spelling, and/or grammatical errors. See, for example, page 19, line 29; page 20, line 5; page 31, line 14; page 34, line 31; page 38, line 29; page 55, lines 26 and 30; page 56, line 2; and page 58, line 4.

Objections to the Claims

2. Claims 35 and 36 are objected to over typographical errors. In claim 35, line 1, “*or*” should be “*of*” and in claim 36, “*peptide*” should be “*peptides*.[”]
3. Claim 54 includes a grammatical error in lines 1 and 2 that does not allow a meaningful interpretation of the claim.

Claims Rejections – 35 U.S.C. 112, first paragraph

4. Claims 28-39 and 48-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for exemplified DNA polymerases and ligases, does not reasonably provide enablement for any combination of catalyst and substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims without undue experimentation.

Several factors are to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any required experimentation is “undue.” These factors include:

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- 1) the breadth of the claims
- 2) the nature of the invention
- 3) the state of the prior art
- 4) the level of one of ordinary skill
- 5) the level of predictability in the art
- 6) the amount of direction provided by the inventor
- 7) the existence of working examples
- 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The rejected claims are drawn to a method for identifying a catalyst of interest from a library of catalysts with no limitation whatsoever on the structure or activity of the catalyst, the structure of the substrate for the catalyst, or the means by which the catalyst and substrate are attached. Catalysts encompassed by the claims include metal catalysts, organometallic catalysts, enzymes of any classification including enzymes that catalyze functionally irreversible reactions, and complex catalysts such as pyruvate dehydrogenase complex, replizomes, and proteosomes, for example.

The state of the prior art was such that methods similar to those claimed had been used for a small number of enzymes and catalytic oligonucleotides. The art was predictable within the bounds of well characterized enzymes or known oligonucleotide sequences for which substrates and reaction mechanisms were known. The art was not predictable with respect to screening for ANY catalyst that could catalyze ANY reaction from ANY substrate to ANY product.

The inventors have provided guidance and examples in the specification, but both are limited to a scope that is much narrower than that claimed. Example 1 in the specification provides a working example for a DNase enzyme that cleaves ssDNA but this exemplified method does not include method steps c) and d) of present claim 28. Example 2 involving a glycosidase enzyme provides only a general concept and lacks the level of detail that would enable one of ordinary skill in the art to use the claimed invention. Example 3 describes how a substrate may be attached to an enzyme in a plasmid peptide system. Example 4 involves a secreted enzyme that is not attached to a substrate or product. Example 5 is a hypothetical example that involves RNase A and does provide guidance with respect to enzyme-substrate and enzyme-product compositions, reaction conditions, and means of separating more active enzyme

from less active enzyme using the method steps of present claim 28. Examples 6 and 7 are hypothetical examples in which the enzyme is DNA polymerase and the substrate is a primer sequence. Guidance with respect to the selection means and some of the reaction conditions are provided. Example 8 provides another hypothetical scenario in which the catalyst (or ribozyme) is a DNA with ligase activity. The example provides guidance for means of separating more active ribozyme from less active ribozyme and corresponding reaction conditions and reagents. Example 9 involves the pre-enrichment of phages.

The examples and references in the specification are enabling for the catalysts and substrates exemplified in examples 6-8 but the guidance provided would not enable one of ordinary skill in the art to extrapolate the use of the claimed method to any catalyst or any enzyme or ribozyme. For example, catalysts that are not enzymes or ribozymes (e.g. metal catalysts and organometallics) require reaction conditions and reagents that have no overlap at all with the guidance provided in the specification. Experimentation would be required to identify appropriate conditions and substrate-product pairs that would allow reversible reactions (which may not be possible for many reactions). For enzyme catalysts too, reactions conditions and substrate-product pairs would have to be identified that would allow either reversible reactions or secondary reactions that operate under conditions compatible with the catalyzed reaction would have to be identified. These tasks would require much research for enzymes (or ribozymes) that are not already well-characterized and for which suitable substrates and products are already known.

Claims Rejections – 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28, 29, 31-33, 48, 49, and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- A. In claim 28, the metes and bounds of the term “*attached to at least one substrate*” are not clear. The term “*attached to*” in this context can be interpreted to mean covalently attached, physically attached , in physical contact with, or non-covalently attached, for example. It is also not clear if “*at least one substrate*” means more than one molecule of the same substrate and/or more then one type of substrate molecule. Clarification is requested.
- B. In claim 28, method step c) recites that at least one attached product is converted to at least one substrate. It is not clear if that substrate is the same as or different from the starting substrate(s) in method step a). Clarification is requested.
- C. In claim 28, method step a), it appears that a reaction is to occur between the catalyst (i.e. a single catalyst or type of catalyst) and at least one substrate. It is not clear if this is the case for all of the catalysts in the library or only one and, if only one, which one. The metes and bounds of a “*reaction*” between a catalyst and a substrate are also not clear. Does this mean, for example, that the catalyst is a covalent catalyst that forms a covalent bond with the substrate or is an acid-base catalysis included even though no bonds are formed between the catalyst and the substrate? Clarification is requested.
- D. In claim 29, the metes and bounds of the term “*biologically amplifiable*” are not clear. Pages 28-29 of the specification list examples of biologically amplifiable and biologically non-amplifiable carrier systems but one of ordinary skill in the art would not be able to determine if, for example, any DNA, RNA, peptide, or protein carrier system would be considered by applicants to be “*biologically amplifiable*” because DNA, RNA and proteins are encoded and can be amplified using biological means.
- E. The term "*flexible linker*" in claim 31 is a relative term, which renders the claim indefinite. The term "*flexible linker*" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Except for the examples provided in the specification, one of ordinary skill would not be able to determine whether a particular linker is a “*flexible*” linker because no standard for measuring flexibility or required minimum flexibility is provided.

F. In claims 32 and 33, the metes and bounds of the term “*carrier system*” are not clear. Page 28 of the specification states that a carrier system is a system or entity that physically connects the catalyst molecule to the substrate or, alternatively, carries information that allows the unambiguous identification of the catalyst molecule. It is not clear what the structural metes and bounds are of an entity that connects physically connects the catalyst molecule to the substrate. It is also not clear what the metes and bounds are of “*information*.” For example, it is not clear if the claim encompasses a molecular tag, fluorescence tags, or if a location in a microtiter well falls into the scope of a “*carrier system*.” It is also not clear, for example, what degree of certainty is required for identification to be considered “*unambiguous*.”

G. In claim 28, it appears that all catalysts catalyze the same reaction and that all of the substrates react to form the same product but the claim does not specifically recite that all of the catalysts in the library catalyze the same reaction and that all of the substrates react to form the same product. Clarification is requested.

H. It is not clear how claim 48 further limits claim 28 because the language in claim 28 does not appear to allow for the catalyst and substrate to be the same chemical substances. Clarification is requested.

I. In claim 49, the metes and bounds of “*enriching*” a library of peptides or polypeptides to obtain a “*library of full-length proteins*” are not clear. It is not clear what methods, for example are considered by applicant to be methods of enrichment. No method steps are provided that would result in full-length proteins, the origins of which are not defined. Clarification is requested.

J. Claim 54 includes a grammatical error in lines 1 and 2 that does not allow a meaningful interpretation of the claim.

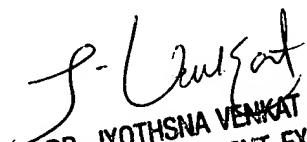
K. In claims 28, 30-33, 48, and 54 the metes and bounds of “*substrate*” and “*catalyst*” are not clear. The term “*substrate*” in the art is normally used only within the context of enzyme catalyzed reactions and not with reactions catalyzed by metals or small molecules. It is not clear if the claim is limited to enzyme catalysts or not. Clarification is requested.

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner can normally be reached on Monday, Tuesday, Friday, and Saturday 8:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.



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Tomas Friend, Ph.D.
18 April 2002